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NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	Jun 03	New e-mail delivery for search results now available
NEWS	4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS	5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS	6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS	7	Sep 03	JAPIO has been reloaded and enhanced
NEWS	8	Sep 16	Experimental properties added to the REGISTRY file
NEWS	9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS	10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS	11	Oct 24	BEILSTEIN adds new search fields
NEWS	12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS	13	Nov 18	DKILIT has been renamed APOLLIT
NEWS	14	Nov 25	More calculated properties added to REGISTRY
NEWS	15	Dec 04	CSA files on STN
NEWS	16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS	17	Dec 17	TOXCENTER enhanced with additional content
NEWS	18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS	19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS	20	Feb 13	CANCERLIT is no longer being updated
NEWS	21	Feb 24	METADDEX enhancements
NEWS	22	Feb 24	PCTGEN now available on STN
NEWS	23	Feb 24	TEMA now available on STN
NEWS	24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS	25	Feb 26	PCTFULL now contains images
NEWS	26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS	27	Mar 20	EVENTLINE will be removed from STN
NEWS	28	Mar 24	PATDPAFULL now available on STN
NEWS	29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS	30	Apr 11	Display formats in DGENE enhanced
NEWS	31	Apr 14	MEDLINE Reload
NEWS	32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS	33	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS	34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS	35	Apr 28	RDISCLOSURE now available on STN
NEWS	36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS	37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS	38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS	39	May 16	CHEMREACT will be removed from STN
NEWS	40	May 19	Simultaneous left and right truncation added to WSCA
NEWS	41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS	42	May 29	PASCAL enhanced with additional data

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT  
 MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),  
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 FILE LAST UPDATED: 29 May 2003 (20030529/ED)

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=> s horsley david/au  
 L1 12 HORSLEY DAVID/AU

=> d all 1-12

L1 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2003 ACS

AN 2003:76597 CAPLUS  
 DN 138:147746  
 TI Naphthoquinone derivatives as inhibitors of tau aggregation for the treatment of Alzheimer's and related neurodegenerative disorders  
 IN Wischik, Claude Michel; **Horsley, David**; Rickard, Janet Elizabeth; Harrington, Charles Robert  
 PA The University Court of the University of Aberdeen, UK  
 SO PCT Int. Appl., 66 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-255  
 ICS A61K031-12  
 CC 1-11 (Pharmacology)  
 Section cross-reference(s): 25

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003007933	A1	20030130	WO 2002-GB3269	20020716
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI GB 2001-17326 A 20010716

OS MARPAT 138:147746

AB Provided are naphthoquinone-type compds. which can be used to modulate the aggregation of protein (e.g. tau) assocd. with neurodegenerative disease (e.g. Alzheimer's disease). Structure-function characteristics for oxidized and reduced naphthoquinone-type compds., such as menadione-related compds., are disclosed. The invention further provides methods of treatment or prophylaxis of neurodegenerative diseases and/or clin. dementias based on the compds. Vitamin K3 (menadione), at 1-2 .mu.M, inhibited proteolytic processing of tau in a cell-based assay.

ST naphthoquinone deriv inhibitor tau aggregation Alzheimer drug; neurodegenerative disorder protein aggregation treatment naphthoquinone deriv; dementia treatment naphthoquinone deriv; Vitamin K3 inhibition tau aggregation

IT Brain, disease

Prion diseases

(Gerstmann-Straussler syndrome, familial; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Alzheimer's disease

(Lewy-body variant; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Mental disorder

(Pick's disease; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Proteins

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); BIOL (Biological study); PROC (Process)

(aggregation assocd. with neurodegenerative disorders, inhibition of; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Tubulins  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
 (binding to tau, inhibition of; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Nerve, disease  
 (corticobasal degeneration; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Disease, animal  
 (degeneration, familial multiple system tauopathy; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Nervous system  
 (degeneration; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Mental disorder  
 (dementia; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Nerve, disease  
 (motor; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Alzheimer's disease  
 Anti-Alzheimer's agents  
 (naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Tau factor  
 RL: ADV (Adverse effect, including toxicity); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)  
 (naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Aggregation  
 (of proteins assocd. with neurodegenerative disorders, inhibition of; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Paralysis  
 (pseudobulbar; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT Structure-activity relationship  
 (tau-aggregation-inhibiting; naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT 83-72-7 130-26-7 483-55-6 1018-78-6 13243-65-7 72520-66-2  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT 58-27-5 84-79-7 84-81-1, Vitamin K2 130-37-0 481-39-0 481-42-5  
 573-20-6 1612-30-2 2197-57-1 2348-82-5 3769-64-0 5416-18-2  
 5690-16-4 7045-83-2 29520-22-7 31519-22-9 34169-62-5 77502-18-2  
 81818-54-4  
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT 130-15-4D, 1,4-Naphthalenedione, derivs.  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (naphthoquinone derivs. as inhibitors of tau aggregation for treatment of Alzheimer's and related neurodegenerative disorders)

IT 494237-53-5

RL: PRP (Properties)

(unclaimed sequence; naphthoquinone derivs. as inhibitors of tau aggregation for the treatment of Alzheimer's and related neurodegenerative disorders)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Allison, A; MEDICAL HYPOTHESES 2001, V57(2), P151 CAPLUS
- (2) Anon; PATENT ABSTRACTS OF JAPAN 2000, V2000(03)
- (3) Bhosale, S; INDIAN JOURNAL OF PHARMACOLOGY 1999, V31(3), P222 CAPLUS
- (4) Brown, D; WO 0191740 A 2001 CAPLUS
- (5) Chayen, J; US 5763479 A 1998 CAPLUS
- (6) Clifford, A; US 2002016372 A1 2002
- (7) Danoun, S; HETEROCYCLIC COMMUNICATIONS 1999, V5(4), P343 CAPLUS
- (8) Gong, C; NEUROSCIENCE 1994, V61(4), P765 CAPLUS
- (9) Kao Corp; JP 11335244 A 1999 CAPLUS
- (10) Ko, L; BRAIN RESEARCH 1997, V760(1-2), P118 MEDLINE
- (11) Kohlmeier, M; DE 19504003 A 1996 CAPLUS
- (12) Kumagai, Y; CHEMICAL RESEARCH IN TOXICOLOGY 1998, V11(6), P608 CAPLUS
- (13) Oommen, E; PHARMACY AND PHARMACOLOGY COMMUNICATIONS 1999, V5(4), P281 CAPLUS
- (14) Takeda Chemical Industries Ltd; EP 0737671 A 1996 CAPLUS
- (15) Wischik, C; WO 9630766 A 1996 CAPLUS

L1 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2003 ACS

AN 2002:790204 CAPLUS

DN 137:303421

TI Method of fabricating suspended microstructures for MEMS, sensors and microactuators

IN **Horsley, David**

PA Hewlett-Packard Company, USA

SO U.S., 11 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM H01L021-311

NCL 438694000

CC 76-14 (Electric Phenomena)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6465355	B1	20021015	US 2001-844356	20010427
	US 2002160611	A1	20021031		
	CN 1384042	A	20021211	CN 2002-106542	20020227
	JP 2003039395	A2	20030213	JP 2002-120034	20020423
	EP 1253108	A2	20021030	EP 2002-253000	20020426
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRAI US 2001-844356 A 20010427

AB A method of fabricating a non-perforated suspended platform on a bonded-substrate is disclosed that eliminates the need to form through holes in the suspended microstructure that reduce the useful surface area. The method includes forming a dielec. layer on a support surface of a base substrate followed by patterning an interface surface of the dielec. layer to define a well feature. The well feature is etched until a well having a depth that leaves a thin protective layer of the dielec. layer covering the support surface. Next a platform substrate is urged into contact with the base substrate followed by annealing the base and platform substrates to fusion bond the interface surface with a mounting surface of the platform substrate. The platform substrate is thinned, to form a membrane over a sealed cavity defined by the well and the mounting surface. The membrane is patterned and etch to form a plurality of trenches that extend through the membrane to the sealed cavity and define a suspended platform and a flexure. A selective etch material such as HF was used to remove the remaining dielec. layer from beneath the platform and the flexures

thereby freeing the suspended platform and the flexures.

ST suspended part MEMS sensor microactuator fabrication

IT Polishing  
 (chem.-mech.; in fabricating suspended microstructures for MEMS, sensors and microactuators)

IT Microactuators  
 Sensors  
 (fabrication of suspended parts for)

IT Joining  
 (fusion; in fabricating suspended microstructures for MEMS, sensors and microactuators)

IT Annealing  
 Dielectric films  
 Etching  
 Grinding (machining)  
 Lithography  
 Membranes, nonbiological  
 Polishing  
 (in fabricating suspended microstructures for MEMS, sensors and microactuators)

IT Micromachines  
 (microelectromech. devices; fabrication of suspended parts for)

IT Etching  
 (selective; in fabricating suspended microstructures for MEMS, sensors and microactuators)

IT 7664-39-3, Hydrogen fluoride, processes  
 RL: CPS (Chemical process); NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)  
 (etchant; in fabricating suspended microstructures for MEMS, sensors and microactuators)

IT 7440-21-3, Silicon, processes 7631-86-9, Silica, processes  
 RL: CPS (Chemical process); DEV (Device component use); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)  
 (in fabricating suspended microstructures for MEMS, sensors and microactuators)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE

- (1) Bashir; US 5747353 A 1998 CAPLUS
- (2) Chau; US 5364497 A 1994
- (3) Core; US 5314572 A 1994 CAPLUS
- (4) Hofmann; US 5637539 A 1997 CAPLUS
- (5) Howe; US 5879963 A 1999
- (6) Macdonald; US 5198390 A 1993 CAPLUS
- (7) Tsang; US 5543013 A 1996 CAPLUS
- (8) Yagi; US 6020215 A 2000 CAPLUS
- (9) Yoshihara; US 5824177 A 1998

L1 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS

AN 2002:736495 CAPLUS

DN 137:244284

TI Neurofibrillary labels

IN Wischik, Claude Michel; Harrington, Charles Robert; Rickard, Janet Elizabeth; **Horsley, David**

PA University of Aberdeen, UK

SO PCT Int. Appl., 160 pp.  
 CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-68  
 ICS C07D277-62; G01N033-58; C07D279-18

CC 9-5 (Biochemical Methods)  
 Section cross-reference(s): 1, 14

FAN.CNT 1



	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002075318	A2	20020926	WO 2002-GB1318	20020320
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	GB 2001-6953	A	20010320		
OS	MARPAT 137:244284				
AB	<p>Disclosed are methods for detg. the stage of neurofibrillary degeneration assocd. with a tauopathy in a subject believed to suffer from the disease, which methods comprise the steps of: (i) introducing into the subject a ligand capable of labeling aggregated paired helical filament (PHF) tau protein, (ii) detg. the presence and/or amt. of ligand bound to extracellular aggregated PHF tau in the medial temporal lobe of the brain of the subject, (iii) correlating the result of the detn. made in (ii) with the extent of neurofibrillary degeneration in the subject. The methods can be used for pre-mortem diagnosis and staging of tauopathies such as Alzheimer's Disease. Preferred ligands include sulfonated-benzothiazole-like compds. and diaminothiazines. Novel ligands (e.g. sulfonated-benzothiazole-like compds.) are also provided. The method may also include the use of "blocking ligands" to block competing binding sites. In other aspects the invention provides in vitro methods for identifying ligands capable of labeling aggregated PHF tau protein, the methods comprising the steps of: (i) providing a first agent suspected of being capable of labeling aggregated PHF tau protein, (ii) contacting (a) a tau protein or a deriv. thereof contg. the tau core fragment bound to a solid phase so as to expose a high affinity tau capture site, with (b) a liq. phase tau protein or deriv. thereof capable of binding to the solid phase tau protein or deriv., and (c) said selected first agent and (d) a second agent known to be tau-tau binding inhibitor, (iii) selecting first agent which fully or partially relieves the inhibition of binding of the liq. phase tau protein or deriv. of (b) to the solid phase tau protein or deriv. of (a) by the inhibitor (d). Ligands may also be tested to confirm that they are not themselves inhibitors.</p>				
ST	neurofibril label drug screening spectrometry tau protein Alzheimer diagnosis				
IT	Nerve				
	(neurofibril; neurofibrillary labels)				
IT	Alzheimer's disease				
	Blood-brain barrier				
	Diagnosis				
	Drug screening				
	Labels				
	Positron-emission tomography				
	Prognosis				
	Spectroscopy				
	pH				
	(neurofibrillary labels)				
IT	Ligands				
	RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)				
	(neurofibrillary labels)				
IT	Tau factor				
	RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)				
	(paired helical filament; neurofibrillary labels)				
IT	Buffers				

(physiol.; neurofibrillary labels)

IT Brain  
(temporal lobe; neurofibrillary labels)

IT 7440-26-8, Technetium, uses  
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)  
(chelators; neurofibrillary labels)

IT 30113-37-2, Primulin 461001-23-0  
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)  
(neurofibrillary labels)

IT 23481-50-7, Dimethylmethylen blue 134652-51-0, 10H-Phenothiazinediamine  
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(neurofibrillary labels)

IT 56-41-7, L-Alanine, properties  
RL: PRP (Properties)  
(tau protein @390; neurofibrillary labels)

IT 56-86-0, L-Glutamic acid, properties  
RL: PRP (Properties)  
(tau protein @391; neurofibrillary labels)

L1 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS

AN 2002:575104 CAPLUS

DN 137:138780

TI Chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases

IN Wischik, Claude Michel; Rickard, Janet Elizabeth; **Horsley, David**; Harrington, Charles Robert; Theuring, Franz; Stamer, Karsten; Zabke, Claudia

PA The University Court of the University of Aberdeen, UK

SO PCT Int. Appl., 123 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K014-705

CC 14-10 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 1, 3

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002059150	A2	20020801	WO 2002-GB5	20020102
	WO 2002059150	A3	20021205		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI GB 2001-119 A 20010103

AB Disclosed are methods of inducing or modeling the pathol. state of an aggregating disease protein (ADP, e.g. tau protein) which is assocd. with a disease state in which the ADP aggregates pathol. (e.g. Alzheimer's disease) through an induced conformational polymn. interaction. The methods are characterized by the step of providing a membrane-localizable fusion protein comprising (i) an aggregating portion, which is derived from the ADP, or from a protein which initiates pathol. aggregation of the ADP, (ii) a heterologous membrane-localizing portion. Membrane-localization of the ADP-based fusion protein is believed to cause the high-affinity capture site of the ADP protein to become exposed such



that aggregation of further ADP, which may be native or heterologous to the system, to be promoted. The method can be carried out in vitro, or in cell- and animal-models, and may be used to screen for modulators of the aggregation process by monitoring aggregation e.g. by monitoring the prodn. of the ADP-related degrdn. products resulting from the aggregation. Also provided are materials, processes for use in or with the methods.

- ST aggregating disease protein membrane localization neurodegenerative disease; drug screening neurodegenerative disease chimeric tau protein; cell animal model disease chimeric tau protein
- IT Genetic element  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(3'-untranslated region; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)
- IT Mental disorder  
(Pick's disease; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)
- IT Prion proteins  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(PrPSc; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)
- IT Prognosis  
(agent; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)
- IT Diagnosis  
(agents; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)
- IT Proteins  
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(aggregating disease; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)
- IT Histochemistry  
(anal.; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)
- IT Alzheimer's disease  
Animal cell  
Animal cell line  
Blood-brain barrier  
Brain  
Cell membrane  
DNA sequences  
Disease models  
Drug screening  
Electron microscopy  
Epitopes  
Fibroblast  
Human

Mammalia  
 Mouse  
 Rat  
 Rodentia  
 (chimeric protein comprising aggregating disease protein and  
 membrane-localizing portion for expressed in cell or animal to identify  
 therapeutic, prognostic and diagnostic agents for neurodegenerative  
 diseases)

IT Fusion proteins (chimeric proteins)  
 Tau factor  
 RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation);  
 BSU (Biological study, unclassified); DGN (Diagnostic use); PRP  
 (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL  
 (Biological study); PREP (Preparation); USES (Uses)  
 (chimeric protein comprising aggregating disease protein and  
 membrane-localizing portion for expressed in cell or animal to identify  
 therapeutic, prognostic and diagnostic agents for neurodegenerative  
 diseases)

IT Nucleic acids  
 RL: ARU (Analytical role, unclassified); BSU (Biological study,  
 unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL  
 (Biological study); USES (Uses)  
 (chimeric protein comprising aggregating disease protein and  
 membrane-localizing portion for expressed in cell or animal to identify  
 therapeutic, prognostic and diagnostic agents for neurodegenerative  
 diseases)

IT Antibodies  
 Primers (nucleic acid)  
 Promoter (genetic element)  
 Tubulins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (chimeric protein comprising aggregating disease protein and  
 membrane-localizing portion for expressed in cell or animal to identify  
 therapeutic, prognostic and diagnostic agents for neurodegenerative  
 diseases)

IT Polymerization  
 (conformational; chimeric protein comprising aggregating disease  
 protein and membrane-localizing portion for expressed in cell or animal  
 to identify therapeutic, prognostic and diagnostic agents for  
 neurodegenerative diseases)

IT Nervous system  
 (degeneration; chimeric protein comprising aggregating disease protein  
 and membrane-localizing portion for expressed in cell or animal to  
 identify therapeutic, prognostic and diagnostic agents for  
 neurodegenerative diseases)

IT Mental disorder  
 (dementia; chimeric protein comprising aggregating disease protein and  
 membrane-localizing portion for expressed in cell or animal to identify  
 therapeutic, prognostic and diagnostic agents for neurodegenerative  
 diseases)

IT Drug delivery systems  
 (implants, embryo; chimeric protein comprising aggregating disease  
 protein and membrane-localizing portion for expressed in cell or animal  
 to identify therapeutic, prognostic and diagnostic agents for  
 neurodegenerative diseases)

IT Antibodies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (monoclonal; chimeric protein comprising aggregating disease protein  
 and membrane-localizing portion for expressed in cell or animal to  
 identify therapeutic, prognostic and diagnostic agents for  
 neurodegenerative diseases)

IT Nerve  
 (neuron; chimeric protein comprising aggregating disease protein and  
 membrane-localizing portion for expressed in cell or animal to identify

therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT Paralysis  
(pseudobulbar; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT Genetic vectors  
(recombinant; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT Genetic element  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(signal sequence; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT Albumins, biological studies  
Globins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(signal; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT Animal  
(transgenic; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT Embryo, animal  
(zygote; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT 444945-70-4P, Protein tau (human clone htau40) 444945-71-5P  
444945-72-6P 444945-73-7P  
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT 444945-55-5 444945-56-6 444945-57-7 444945-58-8 444945-60-2  
444945-61-3 444945-62-4 444945-63-5  
RL: ARU (Analytical role, unclassified); PRP (Properties); ANST (Analytical study)  
(chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT 9014-08-8, Enolase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(neuro-specific; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT 444945-69-1P  
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(nucleotide sequence; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

IT 444949-64-8 444949-65-9

RL: PRP (Properties)

(unclaimed sequence; chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases)

L1 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2003 ACS

AN 2002:539853 CAPLUS

DN 137:88474

TI Drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease

IN Wischik, Claude Michel; **Horsley, David**; Rickard, Janet Elizabeth; Harrington, Charles Robert

PA The University Court of the University of Aberdeen, UK

SO PCT Int. Appl., 137 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N015-85

ICS A61P025-28; G01N033-68

CC 1-11 (Pharmacology)

Section cross-reference(s): 3, 6, 13, 14

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002055720	A2	20020718	WO 2002-GB153	20020115
	WO 2002055720	A3	20021121		
	WO 2002055720	C2	20021227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2001-1049 A 20010115

OS MARPAT 137:88474

AB Disclosed are methods of proteolytically converting a precursor protein (e.g. tau) to a product fragment (e.g. a 12 kd fragment) in a stable cell line, wherein the precursor protein is assocd. with a disease state in which the precursor protein aggregates pathol. (e.g. a tauopathy). Methods comprise providing a stable cell line transfected with nucleic acid encoding a template fragment of the precursor protein such that the template fragment is constitutively expressed in the cell at a level which is not toxic to the cell and the precursor protein, which protein is inducibly expressed in the cell in response to a stimulus, whereby interaction of the template fragment with the precursor protein causes a conformational change in the precursor protein such as to cause aggregation and proteolytic processing of the precursor protein to the product fragment. The method is preferably used to screen for modulators of the aggregation process by monitoring prodn. (or modulation of prodn.) of the product band or bands. Also provided are materials for used in the assays, plus medicaments, and related uses and processes, based on compds. which show high activity in the assay of the invention e.g. reduced diaminothiazines.

ST tau protein aggregation drug screening neurodegenerative disease;  
treatment Alzheimer's Parkinson's disease tau protein proteolysis  
inhibition phenothiazine; sequence tau protein cDNA human

IT Animal cell line  
(3T3, neuronal, tau synthesis in; drug screening for effectors of tau  
protein proteolytic processing and expression systems of controlled  
aggregation in treatment of neurodegenerative disease)

IT Animal cell line  
(3T6, tau synthesis in; drug screening for effectors of tau protein  
proteolytic processing and expression systems of controlled aggregation  
in treatment of neurodegenerative disease)

IT Animal cell line  
(COS-7, tau synthesis in; drug screening for effectors of tau protein  
proteolytic processing and expression systems of controlled aggregation  
in treatment of neurodegenerative disease)

IT Animal cell line  
(N2A, tau synthesis in; drug screening for effectors of tau protein  
proteolytic processing and expression systems of controlled aggregation  
in treatment of neurodegenerative disease)

IT Animal cell line  
(NIE-115, tau synthesis in; drug screening for effectors of tau protein  
proteolytic processing and expression systems of controlled aggregation  
in treatment of neurodegenerative disease)

IT Drug delivery systems  
(Phenothiazine in, for taupathy; drug screening for effectors of tau  
protein proteolytic processing and expression systems of controlled  
aggregation in treatment of neurodegenerative disease)

IT Mental disorder  
(Pick's disease; drug screening for effectors of tau protein  
proteolytic processing and expression systems of controlled aggregation  
in treatment of neurodegenerative disease)

IT Gel electrophoresis  
(SDS-PAGE, tau protein fragments detected using; drug screening for  
effectors of tau protein proteolytic processing and expression systems  
of controlled aggregation in treatment of neurodegenerative disease)

IT Animal cell line  
(SH-SY5Y, tau synthesis in; drug screening for effectors of tau protein  
proteolytic processing and expression systems of controlled aggregation  
in treatment of neurodegenerative disease)

IT Protein motifs  
(core domain of tau protein; drug screening for effectors of tau  
protein proteolytic processing and expression systems of controlled  
aggregation in treatment of neurodegenerative disease)

IT Diffusion  
(correlating inhibitory potential of phenothiazine with; drug screening  
for effectors of tau protein proteolytic processing and expression  
systems of controlled aggregation in treatment of neurodegenerative  
disease)

IT Promoter (genetic element)  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)  
(cytomegalovirus, for tau template fragment synthesis; drug screening  
for effectors of tau protein proteolytic processing and expression  
systems of controlled aggregation in treatment of neurodegenerative  
disease)

IT Nervous system  
(degeneration; drug screening for effectors of tau protein proteolytic  
processing and expression systems of controlled aggregation in  
treatment of neurodegenerative disease)

IT Mental disorder  
(dementia, clin.; drug screening for effectors of tau protein  
proteolytic processing and expression systems of controlled aggregation  
in treatment of neurodegenerative disease)

IT Alzheimer's disease



Drug screening  
 Human  
 Mammalia  
 Nucleic acid hybridization  
 Parkinson's disease  
 (drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Test kits  
 (for stimulating and detecting interaction of tau precursor and template proteins; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Primers (nucleic acid)  
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (for tau cDNA amplification; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT cDNA sequences  
 (for tau factor of human; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Epitopes  
 (human-specific, repeat domain generic, of tau; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Tau factor  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
 (human; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Promoter (genetic element)  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (lac, for synthesis of tau precursor protein; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Antibodies  
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)  
 (monoclonal, to human-specific epitope, core fragment or generic repeat domain of tau protein; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Nerve, disease  
 (motor; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Microtubule  
 (network, tau protein in assembling in; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Animal cell line  
 Fibroblast  
 (neuronal, tau synthesis in; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Protein sequences  
 (of Tau protein; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Aggregation



Molecular association  
 (of tau protein fragments; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Protein engineering  
 (of tau protein truncations; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Molecular cloning  
 Mutagenesis  
 (of tau protein; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Prognosis  
 (of taupathy; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Plasmid vectors  
 (pOPRSVICAT, tau precursor protein synthesis from; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Plasmid vectors  
 (pZeo295-391, tau template fragment synthesis from; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Blood-brain barrier  
 (phenothiazine in treatment of neurodegenerative disease crossing; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Cytomegalovirus  
 (promoter for tau template fragment synthesis; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Post-translational processing  
 (proteolytic, of tau protein core domain; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Paralysis  
 (pseudobulbar; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Anti-Alzheimer's agents  
 Antiparkinsonian agents  
 (screening for; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Brain  
 (tau protein in; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT cDNA  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (tau, of human; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT Antibodies  
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)  
 (to tau protein fragments; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT 442208-27-7  
 RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical

study); USES (Uses)  
 (295 sense primer sequence; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT 442208-28-8  
 RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)  
 (391 antisense primer sequence; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT 442208-25-5  
 RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)  
 (T40-Not I forward primer sequence; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT 442208-26-6  
 RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)  
 (T40-Not I reverse primer sequence; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT 442209-56-5D, Tau factor (human), subfragments are claimed  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (amino acid sequence; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT 50-81-7, Ascorbic acid, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (as stabilizer for phenothiazine in taupathy treatment; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT 6138-09-6, 3,7-Diaminophenothiazine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (asym. methylated, taupathy treatment using; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT 367-93-1, Iptg  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (in lac promoter induction for tau precursor protein synthesis; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT 442209-55-4, DNA (human tau factor cDNA)  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (nucleotide sequence; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

IT 61-73-4, Methylene blue 92-31-9, Tolonium chloride 92-84-2D, Phenothiazine, reduced or Leuco- 531-53-3, Azure A 531-55-5, Azure B 581-64-6, Thionine 23481-50-7, 1,9-Dimethylmethylene blue  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (taupathy treatment using; drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease)

AU Jones, David O.; Mattei, Marie-Genevieve; **Horsley, David**;  
Cowell, Ian G.; Singh, Prim B.

CS Chromatin Function Laboratory, The Babraham Institute, Cambridge, CB2 4AT,  
UK

SO DNA Sequence (2001), 12(3), 147-160  
CODEN: DNSEES; ISSN: 1042-5179

PB Harwood Academic Publishers

DT Journal

LA English

CC 3-3 (Biochemical Genetics)  
Section cross-reference(s): 6, 13

AB The HP1 class of chromobox (Cbx) genes encode an evolutionarily conserved family of proteins involved in the packaging of chromosomal domains into a repressive heterochromatic state. The murine Cbx5, Cbx1 and Cbx3 genes encode the three mouse HP1 proteins, mHP1.alpha., -.beta. and -.gamma. resp. Here, we report the cloning of the mouse Cbx3/HP1.gamma. gene and the chromosomal localization of Cbx3 and three Cbx3-related pseudogenes. The Cbx3 structural gene is located on mouse Chromosome 6, close to the Hoxa cluster. Two Cbx3 processed pseudogenes are sepd. by just 300 bp and are arranged in a head-to-tail configuration on Chromosome 13 while a third pseudogene is found on mouse Chromosome 4. The genomic intron-exon arrangement of Cbx3 is different from the conserved organization of three other mammalian HP1 genes, Cbx1 (mHP1.beta.), CBX3 (hHP1.gamma.), and Cbx5 (mHP1.alpha.) in that Cbx3 lacks an intron that is present in the others.

ST sequence gene pseudogene Cbx3 protein HP1gamma mouse; chromosome mapping  
gene pseudogene Cbx3 HP1 mouse embryogenesis

IT Gene, animal  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(Cbx3; sequence anal., organization and chromosome mapping of mouse gene Cbx3, encoding HP1 protein .gamma. expressed during embryogenesis, and its pseudogenes)

IT Proteins  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(HP1 (heterochromatin-assocd. protein 1), .gamma.; sequence anal., organization and chromosome mapping of mouse gene Cbx3, encoding HP1 protein .gamma. expressed during embryogenesis, and its pseudogenes)

IT Embryo, animal  
(embryogenesis; sequence anal., organization and chromosome mapping of mouse gene Cbx3, encoding HP1 protein .gamma. expressed during embryogenesis, and its pseudogenes)

IT Genetic element  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(exon; sequence anal., organization and chromosome mapping of mouse gene Cbx3, encoding HP1 protein .gamma. expressed during embryogenesis, and its pseudogenes)

IT Evolution  
(mol.; sequence anal., organization and chromosome mapping of mouse gene Cbx3, encoding HP1 protein .gamma. expressed during embryogenesis, and its pseudogenes)

IT Chromosome  
(mouse 13, B; sequence anal., organization and chromosome mapping of mouse gene Cbx3, encoding HP1 protein .gamma. expressed during embryogenesis, and its pseudogenes)

IT Chromosome  
(mouse 4, C3 - C5; sequence anal., organization and chromosome mapping of mouse gene Cbx3, encoding HP1 protein .gamma. expressed during embryogenesis, and its pseudogenes)

IT Chromosome  
(mouse 6, B - C; sequence anal., organization and chromosome mapping of mouse gene Cbx3, encoding HP1 protein .gamma. expressed during embryogenesis, and its pseudogenes)

IT Gene  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study)  
 (pseudogene, Cbx3-ps1, Cbx3-ps2 and Cbx3-ps3; sequence anal.,  
 organization and chromosome mapping of mouse gene Cbx3, encoding HP1  
 protein .gamma. expressed during embryogenesis, and its pseudogenes)

IT DNA sequences  
 Genetic mapping  
 Mouse (Mus musculus)  
 Protein sequences  
 (sequence anal., organization and chromosome mapping of mouse gene  
 Cbx3, encoding HP1 protein .gamma. expressed during embryogenesis, and  
 its pseudogenes)

IT 459876-18-7  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study)  
 (amino acid sequence; sequence anal., organization and chromosome  
 mapping of mouse gene Cbx3, encoding HP1 protein .gamma. expressed  
 during embryogenesis, and its pseudogenes)

IT 344690-09-1, GenBank AJ278616 344690-10-4, GenBank AJ278618  
 344690-11-5, GenBank AJ278619 344690-12-6, GenBank AJ278620  
 344690-13-7, GenBank AJ278621 344690-14-8, GenBank AJ278622  
 344731-44-8, GenBank AJ278617  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study)  
 (nucleotide sequence; sequence anal., organization and chromosome  
 mapping of mouse gene Cbx3, encoding HP1 protein .gamma. expressed  
 during embryogenesis, and its pseudogenes)

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L1 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2003 ACS

AN 2000:642531 CAPLUS

DN 133:346128

TI Conservation of heterochromatin protein 1 function

AU Wang, Guozheng; Ma, Alicia; Chow, Cheok-Man; **Horsley, David**;  
Brown, Nicholas R.; Cowell, Ian G.; Singh, Prim B.

CS Chromatin Function Laboratory, The Babraham Institute, Cambridge, CB2 4AT,  
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SO Molecular and Cellular Biology (2000), 20(18), 6970-6983  
CODEN: MCEBD4; ISSN: 0270-7306

PB American Society for Microbiology

DT Journal

LA English

CC 6-3 (General Biochemistry)

Section cross-reference(s): 10, 13

AB Heterochromatin represents a cytol. visible state of heritable gene repression. In the yeast, *Schizosaccharomyces pombe*, the *swi6* gene encodes a heterochromatin protein 1 (HP1)-like chromodomain protein that localizes to heterochromatin domains, including the centromeres, telomeres, and the donor mating-type loci, and is involved in silencing at these loci. We identify here the functional domains of *swi6p* and demonstrate that the chromodomain from a mammalian HP1-like protein, M31, can functionally replace that of *swi6p*, showing that chromodomain function is conserved from yeasts to humans. Site-directed mutagenesis, based on a modeled three-dimensional structure of the *swi6p* chromodomain, shows that the hydrophobic amino acids which lie in the core of the structure are crit. for biol. function. Gel filtration, gel overlay expts., and mass spectroscopy show that HP1 proteins can self-assoc., and we suggest that it is as oligomers that HP1 proteins are incorporated into heterochromatin complexes that silence gene activity.

ST heterochromatin protein *swi6* structure function yeast

IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(HP1 (heterochromatin-assocd. protein 1), M31 of human;  
characterization of functional domains of yeast heterochromatin protein 1 (gene *swi6*) and homol. with a human heterochromatin protein M31)

IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(HP1 (heterochromatin-assocd. protein 1), gene *swi6* of  
*Schizosaccharomyces*; characterization of functional domains of yeast heterochromatin protein 1 (gene *swi6*) and homol. with a human heterochromatin protein M31)

IT Protein motifs

(heterochromatin assocn.- and nuclear localization domains;  
characterization of functional domains of yeast heterochromatin protein



1 (gene swi6) and homol. with a human heterochromatin protein M31)

IT Chromatin  
(heterochromatin; characterization of functional domains of yeast heterochromatin protein 1 (gene swi6) and homol. with a human heterochromatin protein M31)

IT Self-association  
(of heterochromatin-assocd. proteins; characterization of functional domains of yeast heterochromatin protein 1 (gene swi6) and homol. with a human heterochromatin protein M31)

IT Conformation  
(protein, of swi6/HP1 based on homol. modeling; characterization of functional domains of yeast heterochromatin protein 1 (gene swi6) and homol. with a human heterochromatin protein M31)

IT Gene  
(regulation, by heterochromatin-assocd. proteins; characterization of functional domains of yeast heterochromatin protein 1 (gene swi6) and homol. with a human heterochromatin protein M31)

IT Cell nucleus  
(subcellular localization of swi6/HP1 protein; characterization of functional domains of yeast heterochromatin protein 1 (gene swi6) and homol. with a human heterochromatin protein M31)

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L1 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS

AN 1998:153779 CAPLUS

DN 128:255518

TI The M31 gene has a complex developmentally regulated expression profile and may encode alternative protein products that possess diverse subcellular localization patterns

AU Peterson, Karen; Wang, Guozheng; **Horsley, David**; Richardson, Jenny C.; Sapienza, Carmen; Latham, Keith E.; Singh, Prim B.

CS Ludwig Institute for Cancer Research, San Diego Branch, La Jolla, CA, 92093-0660, USA

SO Journal of Experimental Zoology (1998), 280(4), 288-303  
CODEN: JEZAO; ISSN: 0022-104X

PB Wiley-Liss, Inc.

DT Journal

LA English

CC 13-3 (Mammalian Biochemistry)

Section cross-reference(s): 3

AB HP1-like chromobox genes comprise an evolutionarily conserved family of genes that encode components of centromeric heterochromatin. To investigate the role of the murine HP1-like gene, M31, in heterochromatin formation the authors have isolated its gene and characterized its transcripts and protein products. PCR products that represent M31 transcripts were detected at the one-cell stage and were maternal in origin. Maternal provision of M31 transcripts may reflect a need for M31 in the formation of a functional centromere in order that there is proper segregation of chromosomes during the early cleavage divisions; studies in fission yeast and Drosophila have suggested a crucial role for HP1-like genes in centromere function. There are three protein products encoded by the M31 gene. Surprisingly, the two smaller products are found almost exclusively in the cytoplasm.

ST M31 gene cloning expression development mouse

IT Gene, animal

RL: PRP (Properties)

(M31 chromobox; the M31 gene has a complex developmentally regulated expression profile and may encode alternative protein products that

possess diverse subcellular localization patterns)

IT Gene, animal  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (M31; the M31 gene has a complex developmentally regulated expression profile and may encode alternative protein products that possess diverse subcellular localization patterns)

IT Embryo, animal  
 (embryogenesis; the M31 gene has a complex developmentally regulated expression profile and may encode alternative protein products that possess diverse subcellular localization patterns)

IT Proteins, specific or class  
 RL: PRP (Properties)  
 (gene M31; the M31 gene has a complex developmentally regulated expression profile and may encode alternative protein products that possess diverse subcellular localization patterns)

IT Chromatin  
 (heterochromatin; the M31 gene has a complex developmentally regulated expression profile and may encode alternative protein products that possess diverse subcellular localization patterns)

IT Centromeres  
 Cytoplasm  
 Mouse  
 cDNA sequences  
 (the M31 gene has a complex developmentally regulated expression profile and may encode alternative protein products that possess diverse subcellular localization patterns)

IT 173079-19-1, GenBank X95400 173079-20-4, GenBank X95397 173079-21-5, GenBank X95398 173079-22-6, GenBank X95399  
 RL: PRP (Properties)  
 (nucleotide sequence; the M31 gene has a complex developmentally regulated expression profile and may encode alternative protein products that possess diverse subcellular localization patterns)

L1 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2003 ACS

AN 1998:36852 CAPLUS

DN 128:63271

TI Process Plant Commissioning, Second Edition.

AU **Horsley, David**; Editor

CS UK

SO (1998) Publisher: (Inst. Chem. Eng., Rugby, UK), 115 pp.

DT Book

LA English

CC 47-10 (Apparatus and Plant Equipment)

AB Unavailable

ST book process plant commissioning

IT Chemical industry  
 (commissioning of process plant)

L1 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2003 ACS

AN 1993:145563 CAPLUS

DN 118:145563

TI A monoclonal antibody, JIM 84, recognizes the Golgi apparatus and plasma membrane in plant cells

AU **Horsley, David**; Coleman, Julian; Evans, David; Crooks, Kim; Peart, Jan; Satiat-Jeunemaitre, Beatrice; Hawes, Chris

CS Sch. Biol. Mol. Sci., Oxford Polytech., Headington/Oxford, OX3 0BP, UK

SO Journal of Experimental Botany (1993), 44(Suppl.), 223-9

CODEN: JEBOA6; ISSN: 0022-0957

DT Journal

LA English

CC 15-3 (Immunochemistry)

AB A monoclonal antibody, JIM 84, was raised against a carrot coated vesicle fraction. Immunofluorescence and immunogold labeling show that the JIM 84

epitope is localized in all the cisternae of the Golgi app. and is assocd. with the plasma membrane in a range of different plant cell types. Periodate treatment of coated vesicle preps. monitored by ELISA suggest that the JIM 84 epitope is a glycoprotein, while SDS-PAGE gels of carrot and maize microsomal preps. show that the antibody recognizes peptides of Mr 25,000-70,000.

ST monoclonal antibody Golgi cell membrane plant  
IT Carrot  
    (monoclonal antibody to cell membrane and Golgi body of cells of)  
IT Plant cell  
    (monoclonal antibody to components of)  
IT Cell membrane  
    Golgi apparatus  
    (of plant cells, monoclonal antibody to)  
IT Antibodies  
RL: BIOL (Biological study)  
    (monoclonal, JIM 84, Golgi body and cell membrane of plant cells  
    recognition by)

L1 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2003 ACS  
AN 1993:142102 CAPLUS  
DN 118:142102  
TI Molecular and structural studies of plant clathrin coated vesicles  
AU **Horsley, David**  
CS Univ. Oxford, Oxford, UK  
SO (1991) 284 pp. Avail.: Univ. Microfilms Int., Order No. BRD-95123  
From: Diss. Abstr. Int. B 1992, 52(11), 5668  
DT Dissertation  
LA English  
CC 6-7 (General Biochemistry)  
Section cross-reference(s): 11  
AB Unavailable  
ST plant clathrin coated vesicle  
IT Plant  
    (clathrin-coated vesicles of, mol. and structural studies of)  
IT Clathrins  
RL: BIOL (Biological study)  
    (coated vesicle, mol. and structural studies of, of plant)  
IT Organelle  
    (coated vesicle, of plant, mol. and structural studies of)

L1 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2003 ACS  
AN 1987:572786 CAPLUS  
DN 107:172786  
TI Structure and molecular organization of higher plant coated vesicles  
AU Coleman, Julian; Evans, David; Hawes, Chris; **Horsley, David**;  
Cole, Louise  
CS Dep. Plant Sci., Oxford Univ., Oxford, OX1 3RA, UK  
SO Journal of Cell Science (1987), 88(1), 35-45  
CODEN: JNCSAI; ISSN: 0021-9533  
DT Journal  
LA English  
CC 11-8 (Plant Biochemistry)  
Section cross-reference(s): 6  
AB Suspension-cultured cells of carrot (*Daucus carota*) contain 3 populations of coated vesicles, assocd. with the plasma membrane (84-91 nm diam.), Golgi dictyosomes, and the partially coated reticulum (61-73 nm diam.). These were obsd. by thin sectioning, dry-cleaving and rapid-freeze deep-etching of cells. Dissocn. of clathrin coats with Tris, released triskelions that were morphol. identical with those from mammalian tissue. The triskelion arm length of carrot clathrin was greater (61 vs. 44-50 nm), but packaging results in clathrin cages of pentagons and hexagons of similar size to those from mammalian cells. SDS-PAGE of tris-released triskelion preps. revealed a complex of 3 polypeptides of 190, 60 and

57(.times.103)Mr. The 190 .times. 103Mr protein is the plant clathrin heavy chain, slightly larger than the mammalian heavy chain. The 60 and 57(.times.103)Mr bands showed the same sensitivities to protease treatment as mammalian light chains. triskelion prepns. contg. these three proteins reassembled into polyhedral cages. These results are discussed in relation to the structural organization of coated vesicles and clathrin cages in other systems.

ST carrot coated vesicle clathrin

IT Carrot

(coated vesicles of, structure and mol. organization of)

IT Clathrins

RL: PROC (Process)

(of carrot coated vesicles, characterization of)

IT Organelle

(coated vesicle, of carrot, structure and mol. organization of)

=> d ti 1-12

L1 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI Naphthoquinone derivatives as inhibitors of tau aggregation for the treatment of Alzheimer's and related neurodegenerative disorders

L1 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI Method of fabricating suspended microstructures for MEMS, sensors and microactuators

L1 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI Neurofibrillary labels

L1 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI Chimeric protein comprising aggregating disease protein and membrane-localizing portion for expressed in cell or animal to identify therapeutic, prognostic and diagnostic agents for neurodegenerative diseases

L1 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI Drug screening for effectors of tau protein proteolytic processing and expression systems of controlled aggregation in treatment of neurodegenerative disease

L1 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI The gene and pseudogenes of Cbx3/mHP1.gamma.

L1 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI Conservation of heterochromatin protein 1 function

L1 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI The M31 gene has a complex developmentally regulated expression profile and may encode alternative protein products that possess diverse subcellular localization patterns

L1 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI Process Plant Commissioning, Second Edition.

L1 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI A monoclonal antibody, JIM 84, recognizes the Golgi apparatus and plasma membrane in plant cells

L1 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI Molecular and structural studies of plant clathrin coated vesicles

L1 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2003 ACS

TI Structure and molecular organization of higher plant coated vesicles

=> SET SMA OFF

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=> SEL RAN.CAPLUS(1) L1 2

E1 THROUGH E1 ASSIGNED

=> SET SMA LOGIN

SET COMMAND COMPLETED

=> S E1

L2 1 "1998:293101"/AN

=> D L2 BIB,ABS

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

AN 1998:293101 CAPLUS

DN 128:329882

TI Making a surface micromachined accelerometer using silicon-on-insulator technology

IN Bashir, Rashid; Kabir, Abul E.

PA National Semiconductor Corp., USA

SO U.S., 16 pp., Division of U.S. Ser. No. 633,197, abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5747353	A	19980505	US 1997-814352	19970311
PRAI	US 1996-633197		19960416		

AB In making a surface micromachined accelerometer using a Si-on-insulator (SOI) wafer structure, both the acceleration (or deceleration) sensor and assocd. signal-conditioning circuitry are monolithically fabricated on the same substrate. The top Si layer of the SOI wafer is used as the sensing member, corresponding to the movable, common electrode of a differential capacitor pair. The components of the signal-conditioning circuitry are fabricated in the SOI layer using std. SOI processing techniques. Because the top Si layer is single-crystal Si, it does not suffer from the stress-related warping common with polysilicon members. Because the method described is compatible with bipolar, BiCMOS, or CMOS process flows, it may be used to fabricate faster and lower-noise signal-conditioning circuitry than can be obtained using current techniques for making monolithic accelerometers.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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